(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 4 October 2001 (04.10.2001)

PCT

(10) International Publication Number WO 01/72711 A1

(51) International Patent Classification⁷: C07D 215/54, 409/04, 401/04, 401/06, 405/04, 405/14, 409/14, 401/12, 401/10, 401/14, 405/12, 471/04, A61K 31/4706, 31/4709, A61P 35/00 // (C07D 471/04, 221:00, 221:00)

(21) International Application Number: PCT/US01/09966

(22) International Filing Date: 28 March 2001 (28.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

09/535,843 28 March 2000 (28.03.2000) US

(71) Applicant: AMERICAN HOME PRODUCTS COR-PORATION [US/US]; Five Giralda Farms, Madison, NJ 07940 (US).

(72) Inventors: BOSCHELLI, Diane, Harris; 3A Elyse Drive, New City, NY 10956 (US). WANG, Yanong; 14 Blue Heron Road, Nanuet, NY 10954 (US). BOSCHELLI, Frank, Charles; 3A Elyse Drive, New City, NY 10956 (US). BERGER, Dan, Maarten; 6 Irion Drive, New City, NY 10956 (US). ZHANG, Nan; 214-10 64 Avenue, Bayside, NY 11364 (US). POWELL, Dennis, William; 50 Maple Moor Lane, Cortlandt Manor, NY 10567 (US). YE, Fei; 1 South Lexow Avenue, Manuet, NY 10954 (US). YAMASHITA, Ayako; 52 Dwight Place #F, Englewood, NJ 07631 (US). DEMORIN, Frenel, Fils; 3023 Mulberry

Circle, Thousand Oaks, CA 91360 (US). WU, Biqi; Apt. 2F, 24 Old Middletown Road, Manuet, NY 10954 (US). TSOU, Hwei-Ru; 7 Beverly Place, New City, NY 10956 (US). OVERBEEK-KLUMPERS, Elsebe, Geraldine; Sportlaan 179, NL-7691 BK Bergentheim (NL). WISS-NER, Allan; 31 Wood Avenue, Ardsley, NY 10502 (US).

(74) Agents: BERG, Egon, E.; American Home Products Corporation, Patent Law Department, Five Giralda Farms, Madison, NJ 07054 et al. (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

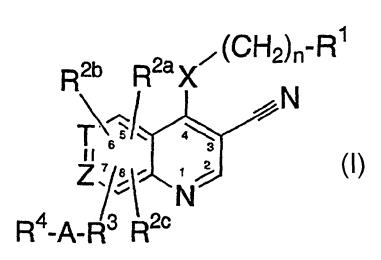
(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 3-CYANOQUINOLINES,3-CYANO-1,6-NAPHTHYRIDINES, AND 3-CYANO-1,7-NAPHTHYRIDINES AS PROTEIN KINASE INHIBITORS



(57) Abstract: Compounds of Formula (I), having the structure or a pharmaceutically salt thereof are useful as antineoplastic agents and in the treatment of osteoporosis and polycystic kidney disease.



WO 01/72711

3-CYANO-1,7-NAPHTHYRIDINES AS PROTEIN KINASE INHIBITORS

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to 3-cyanoquinoline, 3-cyano-1,6-naphthyridine and 3-cyano-1,7-naphthyridine containing compounds as well as their pharmaceutically acceptable salts. The compounds of the present invention inhibit the activity of protein kinases that are required for cell growth and differentiation. The compounds of this invention are therefore useful for the treatment of certain diseases that result from activity of these protein kinases. The compounds of this invention are anticancer agents and are useful for the treatment of cancer in mammals. In addition, the compounds of this invention are useful for the treatment of polycystic kidney disease in mammals. The compounds of this invention may also be used in the treatment of osteoporosis. This invention also relates to the manufacture of said compounds, their use for the treatment of cancer, polycystic kidney disease and osteoporosis, and the pharmaceutical preparations containing them.

2. Description of the Prior Art

Protein kinases are enzymes that catalyze the transfer of a phosphate group from ATP to an amino acid residue, such as tyrosine, serine, threonine, or histidine on a protein. Regulation of these protein kinases is essential for the control of a wide variety of cellular events including proliferation and migration. Specific protein kinases have been implicated in diverse conditions including cancer [Traxler, P. M., Exp. Opin. Ther. Patents, 8, 1599 (1998); Bridges, A. J., Emerging Drugs, 3, 279 (1998)], restenosis [Mattsson, E., Trends Cardiovas. Med. 5, 200 (1995); Shaw, Trends Pharmacol. Sci. 16, 401 (1995)], atherosclerosis [Raines, E. W., Bioessays, 18, 271 (1996)], angiogenesis [Shawver, L. K., Drug Discovery Today, 2, 50

2

(1997); Folkman, J., *Nature Medicine*, 1, 27 (1995)] and osteoporosis [Boyce, J. Clin. Invest., 90, 1622 (1992)].

Tyrosine kinases (TKs) are divided into two classes: the non-transmembrane TKs and transmembrane growth factor receptor TKs (RTKs). Growth factors, such as epidermal growth factor (EGF), bind to the extracellular domain of their partner RTK on the cell surface which activates the RTK, initiating a signal transduction cascade that controls a wide variety of cellular responses including proliferation and migration. The overexpression of EGF and also of members of the epidermal growth factor receptor (EGFr) family, which includes EGF-r, erbB-2, erbB-3 and erbB-4, is implicated in the development and progression of cancer [Rusch, V., Cytokine Growth Factor Rev., 7, 133 (1996), Davies, D. E., Biochem. Pharmacol., 51, 1101 (1996) and Modjtahedi, E., Int. J. Oncol., 4, 277 (1994)]. Specifically, over expression of the receptor kinase product of the erbB-2 oncogene has been associated with human breast and ovarian cancers [Slamon, D. J., Science, 244, 707 (1989) and Slamon, D. J., Science, 235, 177 (1987)]. Upregulation of EGFr kinase activity has been associated with epidermoid tumors [Reiss, M., Cancer Res., 51, 6254 (1991)], breast tumors [Macias, A., Anticancer Res., 7, 459 (1987)], and tumors involving other major organs [Gullick, W.J., Brit. Med. Bull., 47, 87 (1991)].

It is also known that deregulation of EGF receptors is a factor in the growth of epithelial cysts in the disease described as polycystic kidney disease [Du, J., Amer. J. Physiol., 269 (2 Pt 1), 487 (1995); Nauta, J., Pediatric Res., 37(6), 755 (1995); Gattone, V. H., Developmental Biology, 169(2), 504 (1995); Wilson, P. D., Eur. J. Cell Biol., 61(1), 131, (1993)]. Compounds which inhibit the catalytic function of the EGF receptors, may consequently be useful for the treatment of this disease.

In addition to EGFr, there are several other RTKs including FGFr, the receptor for fibroblast growth factor (FGF); flk-1, also known as KDR, and flt-1, the receptors for vascular endothelial growth factor (VEGF); and PDGFr, the receptor for platelet derived growth factor (PDGF). The formation of new blood vessels, a process known as angiogenesis, is essential for tumor growth. Two natural

3

angiogenesis inhibitors, angiostatin and endostatin, dramatically inhibited the growth of a variety of solid tumors. [O'Reilly, M. S., *Cell*, 79, 315 (1994); O'Reilly, M. S., *Nature Medicine*, 2, 689 (1996); O'Reilly, M. S., *Cell*, 88, 277 (1997)]. Since FGF and VEGF are known to stimulate angiogenesis, inhibition of the kinase activity of their receptors should block the angiogenic effects of these growth factors. In addition, the receptor tyrosine kinases tie-1 and tie-2 also play a key role in angiogenesis [Sato, T. N., *Nature*, 376, 70 (1995)]. Compounds that inhibit the kinase activity of FGFr, flk-1, flt-1, tie-1 or tie-2 may inhibit tumor growth by their effect on angiogenesis.

PDGF is a potent growth factor and chemoattractant for smooth muscle cells (SMCs) and the renarrowing of coronary arteries following angioplasty is due in part to the enhanced proliferation of SMCs in response to increased levels of PDGF. Therefore, compounds that inhibit the kinase activity of PDGFr may be useful in the treatment of restenosis. In addition, since PDGF and PDGFr are overexpressed in several types of human gliomas, small molecules capable of suppressing PDGFr activity, have potential utility as anticancer therapeutics [Nister, M., *J. Biol. Chem.* 266, 16755 (1991); Strawn, L. M., *J. Biol. Chem.* 269, 21215 (1994)].

Other RTKs that could potentially be inhibited by compounds of this invention include colony stimulating factor receptor, the nerve growth factor receptors (trkA, trkB and trkC), the insulin receptor, the insulin-like growth factor receptor, the hepatocyte growth factor receptor and the erythropoietin-producing hepatic cell receptor (EPH).

In addition to the RTKs there is another family of TKs termed the cytoplasmic protein or non-receptor TKs. The cytoplasmic protein TKs have intrinsic kinase activity, are present in the cytoplasm and nucleus, and participate in diverse signaling pathways. There are a large number of non-receptor TKs including Abl, Jak, Fak, Syk, Zap-70 and Csk. However, the major family of cytoplasmic protein TKs is the Src family which consists of at least eight members (Src, Fyn, Lyn, Yes, Lck, Fgr, Hck and Blk) that participate in a variety of signaling pathways [Schwartzberg, P. L., *Oncogene*, 17, 1463 (1998)]. The prototypical member of this

4

tyrosine kinase family is Src, which is involved in proliferation and migration responses in many cell types. Src activity has been shown to be elevated in breast, colon (~90%), pancreatic (>90%) and liver (>90%) tumors. Greatly increased Src activity is also associated with metastasis (>90%) and poor prognosis. Antisense Src message impedes growth of colon tumor cells in nude mice [Staley, C. A., *Cell Growth Differentiation*, 8, 269 (1997)], suggesting that Src inhibitors should slow tumor growth. In addition to its role in cell proliferation, Src also acts in stress response pathways, including the hypoxia response. Nude mice studies with colon tumor cells expressing antisense Src message have reduced vascularization [Ellis, L. M., *J. Biol. Chem.*, 273, 1052 (1998)], which suggests that Src inhibitors would be anti-angiogenic as well as anti-proliferative.

In addition to its role in cancer, Src also appears to play a role in osteoporosis. Mice genetically engineered to be deficient in Src production were found to exhibit osteopetrosis, the failure to resorb bone [Soriano, P., Cell, 64, 693 (1991); Boyce, B. F., J. Clin., Invest., 90, 1622 (1992)]. This defect was characterized by a lack of osteoclast activity. Since osteoclasts normally express high levels of Src, inhibition of Src kinase activity may be useful in the treatment of osteoporosis [Missbach, M., Bone, 24, 437 (1999)].

Two members of the cytoplasmic protein TKs, lck and ZAP-70 are predominately expressed on T-cells and natural killer (NK) cells. Inhibitors of these kinases can suppress the immune system and therefore have possible therapeutic potential to treat autoimmune diseases such as rheumatoid arthritis, sepsis, and transplant rejection [Myers, M., Current Pharm. Design, 3, 473 (1997)].

Besides TKs, there are additional kinases including those that phosphorylate serine and/or threonine residues on proteins. A major pathway in the cellular signal transduction cascade is the mitogen-activated protein kinase (MAPK) pathway which consists of the MAP kinase kinases (MAPKK), including mek, and their substrates, the MAP kinases (MAPK), including erk [Seger, R., FASEB, 9, 726 (1995)]. When activated by phosphorylation on two serine residues by upstream kinases, such as members of the raf family, mek catalyzes the phosphorylation of

5

threonine and tyrosine residues on erk. The activated erk then phosphorylates and activates both transcription factors in the nucleus and other cellular targets. Over-expression and/or over-activation of mek or erk is associated with various human cancers [Sivaraman, V. S., *J. Clin. Invest.*, *99*, 1478 (1997)].

As mentioned above, members of the raf family of kinases phosphorylate serine residues on mek. There are three serine/threonine kinase members of the raf family known as a-raf, b-raf and c-raf. While mutations in the raf genes are rare in human cancers, c-raf is activated by the ras oncogene which is mutated in a wide number of human tumors. Therefore inhibition of the kinase activity of c-raf may provide a way to prevent ras mediated tumor growth [Campbell,S. L., *Oncogene*, 17, 1395 (1998)].

The cyclin-dependent kinases (cdks), including cdc2/cyclin B, cdk2/cyclin A, cdk2/cyclin E and cdk4/cyclin D, and others, are serine/threonine kinases that regulate mammalian cell division. Increased activity or activation of these kinases is associated with the development of human tumors [Garrett, M. D., *Current Opin. Genetics Devel.*, 9, 104 (1999); Webster, K. R., *Exp. Opin. Invest. Drugs*, 7, 865 (1998)]. Additional serine/threonine kinases include the protein kinases A, B, and C. These kinases are known as PKA or cyclic AMP-dependent protein kinase, PKB or Akt, and PKC, and all three play key roles in signal transduction pathways responsible for oncogenesis [Glazer, R. I., *Current Pharm. Design*, 4(3), 277 (1998)]. Compounds capable of inhibiting the kinase activity of mek, erk, raf, cdc2/cyclin B, cdk2/cyclin A, cdk2/cyclin E, cdk4/cyclin D, PKA, Akt or PKC may be useful in the treatment of diseases characterized by abnormal cellular proliferation, such as cancer.

The serine/threonine kinase UL97 is a virion-associated protein kinase which is required for the replication of human cytomegalovirus [Wolf, D.G., *Arch. Virology 143(6)*, 1223 (1998) and He, Z., *J. Virology*, 71, 405(1997)]. Compounds capable of inhibiting the kinase activity of UL97 may be useful antiviral therapeutics. Since certain bacteria require the action of a histidine kinase for

6

proliferation [Loomis, W. F., *J. Cell Sci.*, 110, 1141 (1997)], compounds capable of inhibiting such histidine kinase activity may be useful antibacterial agents.

Some 3-cyanoquinoline derivatives are inhibitors of tyrosine kinases and are described in the application WO9843960 (US 6,002,008). These 3-cyanoquinolines may be substituted at carbon-5 through carbon-8 with an unsubstituted phenyl, alkene or alkyne group. A 3-cyanoquinoline with a 4-(2-methylanilino) substituent having gastric (H⁺/K⁺)-ATPase inhibitory activity at high concentrations has been described [Ife, R., *J. Med. Chem.*, *35(18)*, 3413 (1992)].

Some 3-cyanoquinolines are claimed as inhibitors of tumor necrosis factor (TNF) or phosphodiesterase IV. The application WO982007 claims 3cyanoquinolines that may be unsubstituted at carbon-2 and substituted at carbon-4 with an aryloxy, cycloalkoxy, heteroaryloxy or anilino group. However these compounds must contain at carbon-8 a hydroxy, thioalkyl, alkoxy of 1 to 6 carbon atoms or cycloalkoxy group optionally substituted with one or more halogens. These compounds must also contain at carbon-5 an imidazole, oxazole, or thiazole ring attached to the quinoline ring at carbon-2 and this hereroaryl ring must be fused to a 6-membered aromatic ring that may contain 1 or 2 nitrogen atoms in the ring. The application WO9857936 also claims 3-cyanoquinolines as inhibitors of tumor necrosis factor (TNF) or phosphodiesterase IV. These compounds may be unsubstituted at carbon-2 but must contain at carbon-8 a hydroxy, thioalkyl, alkoxy of 1 to 6 carbon aroms or cycloalkoxy group optionally substituted with one or more halogens. These compounds must contain at carbon-5 an aryl or heteroaryl ring that may be substituted. In addition these compounds may contain a aryloxy, cycloalkoxy, or heteroaryloxy group at carbon-4. However when an amino group is present at carbon-4 the amino group must be substituted by an alkylcarbonyl, alkoxycarbonyl, arylsulfonyl, heteroarylsulfonyl, heterocyclosulfonyl, arylcarbonyl, heteroarylcarbonyl, heterocyclocarbonyl or alkylsulfonyl group.

The applications WO9744036 and WO9744322 claim additional 3-cyanoquinolines as inhibitors of tumor necrosis factor (TNF) or phosphodiesterase

7

IV but these applications do not claim the substituents at carbon-5 through carbon-8 of the 3-cyanoquinolines claimed herein.

The applications WO9404526 and WO9404527 claim 3-cyanoquinolines as pesticides. These 3-cyanoquinolines may be unsubstituted at carbon-2, but differ from the compounds claimed herein that they must contain at carbon-4 a group of formula -Y(CH₂) ₂-phenyl, -Y(CH₂) ₂-pyridine or -Y(CH₂) ₂-pyridazine, where Y is O, CH₂, NH or N-alkyl. These applications also do not claim the substituents at carbon-5 through carbon-8 of the 3-cyanoquinolines claimed herein.

A series of patent applications, WO9719927, WO9602509, and WO9532948 claim 3-cyanoquinolines as neurokinin inhibitors. However these compounds must contain at carbon-4 of the quinoline a group of the formula C(X)NRR wherein X is O, S or N-CN and in addition carbon-2 of the quinoline can not be unsubstituted.

Several patents and patent applications claim 3-cyanoquinolines as inhibitors of leukotriene biosynthesis. While some of these, including US5232916, US5104882, EP349062 and DE19532714, claim compounds with the substituents at carbon-4 and at carbon-5 through carbon-8 of the cyanoquinoline claimed herein, all of the compounds must contain a substituent at carbon-2.

Several patent applications claim 3-cyanoquinolines as angiotensin II antagonists. EP499415 claims 3-cyanoquinolines, unsubstituted at carbon-2 and substituted at carbon-4 with a group of the formula NRCH₂Ph, wherein R is H or lower alkyl and Ph is phenyl which must be substituted by a tetrazole, C(O)NHtetrazole or other specified groups. This application does not claim the substituents at carbon-5 through carbon-8 of the 3-cyanoquinolines claimed herein. A series of patent applications EP527534, EP456442 and GB2264710 claim 3-cyanoquinolines, unsubstituted at carbon-2 and substituted at carbon-4 with a group of the formula OCH₂Ph, but these applications do not claim the substituents at carbon-5 through carbon-8 of the 3-cyanoquinolines claimed herein.

US patent 5480883 describes a series of compounds including quinolines as tyrosine kinase inhibitors. These quinoline compounds are unsubstituted at carbon-3. Patent application WO9609294 describes quinazolines and quinolines substituted at

8

carbon-4 by anilino, phenoxy and thiophenoxy groups as tyrosine kinase inhibitors, however the quinoline compounds are unsubstituted at carbon-3. US patent 5650415 describes quinolines substituted at carbon-4 by a benzylamino or benzylthio group as tyrosine kinase inhibitors. These quinolines however must contain an ethyl ester group at carbon-3. Additional quinoline compounds substituted with an ethyl ester at carbon-3 and an anilino group at carbon-4 are claimed in US patent 4343804 as antisecretory and antiulcer compounds.

Patent application WO9813350 describes 3-fluoroquinolines, quinolines, 1,6-naphthyridines and 1,7-naphthyridines substituted at carbon-4 by anilino, phenoxy and thiophenoxy groups as tyrosine kinase inhibitors, but does not include the 3-cyano group contained in the quinoline, 1,6-naphthyridine and 1,7-naphthyridine compounds of the present invention.

Several patents and patent applications disclose quinazolines with anilino groups at carbon-4 and substituted at carbons-5 to 8 with a phenyl, naphthyl, alkene, alkyne or a 5-6 membered heteroaryl group as kinase inhibitors. US patent 5814630 describes quinazolines substituted at carbon-7 with a phenyl, naphthyl or 5-6 membered heteroaromatic ring. US patent 5866572 describes 4-anilinoquinazolines substituted at carbon-6 with a phenyl, naphthyl or 5-6 membered heteroaryl group that may be directly attached to the quinazoline or attached via a carbonyl, alkyl or hydroxymethylene linker. US patent 5955464 describes 4-anilinoquinazolines substituted at carbon-6 by a nitrogen containing heteroaryl group that is linked to the quinazoline via a nitrogen atom. The application EP837063 describes quinazolines that are substituted at carbons-5 to 8 with one or more optionally substituted 5- or 6-membered heteroaryl, or phenyl rings either directly attached to the quinazoline or attached via an alkene or alkyne linker.

Additionally, the application WO9802434 describes quinazolines and quinolines, as kinase inhibitors, unsubstituted at carbon-3, that are substituted at carbons -5 to 8 with one or more optionally substituted 5- or 6-membered heteroaryl or phenyl rings. Patent applications WO9802437 and WO9935146 further describe ring systems, including quinolines, 1,6-naphthyridines and 1,7-naphthyridines with

9

anilino groups at carbon-4 and substituted at carbons-5 to 8 with one or more optionally substituted 5- or 6-membered heteroaryl or phenyl rings, as kinase inhibitors and which do not disclose the 3-cyano group of the present invention.

The compounds of the present invention are 3-cyanoquinolines with a suitably substituted heteroaryl, bicyclic heteroaryl, aryl, alkene or alkyne group at carbon-5, carbon-6, carbon-7, or carbon-8. Alternative names for 3-cyanoquinolines include 3-quinolinecarbonitriles and quinoline-3-carbonitriles. Also included in the present invention, are 3-cyano-1,6-naphthyridines with a suitably substituted heteroaryl, bicyclic heteroaryl, alkene or alkyne group at carbon-5, carbon-7, or carbon-8 and 3-cyano-1,7-naphthyridines with a suitably substituted heteroaryl, bicyclic heteroaryl, aryl, alkene or alkyne group at carbon-5, carbon-6, or carbon-8. The compounds of the present invention inhibit the activity of protein kinases that are required for cell growth and differentiation and are therefore useful for the treatment of certain diseases that result from activity of these protein kinases. The compounds of this invention are anti-cancer agents and are useful for the treatment of cancer in mammals. Further, the compounds of this invention are useful for the treatment of polycystic kidney disease in mammals.

SUMMARY OF THE INVENTION

In accordance with the present invention there is provided compounds represented by Formula (I):

wherein:

X is -NH-, -NR⁵-, -O-, or -S(O)_m-; n is an integer of 0 or 1; m is an integer of 0 to 2; q is an integer of 0 to 5; p is an integer of 2 to 5; s is an integer of 0 to 5; r is an integer of 0 to 5;

J is halogen;

A is $-(C(R^9)_2)_{r^-}$, $-C(O)_{r^-}$, $-C(O)(C(R^9)_2)_{r^-}$, $-(C(R^9)_2)_{r^-}$, $-(C(O)_{r^-}$, -cycloalkyl- or is absent; T and Z are each independently carbon or N, provided that both T and Z are not simultaneously N;

 R^1 is selected from a cycloalkyl ring of 3 to 10 carbon atoms, optionally substituted with one or more independently selected alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q,

11:

 $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^{7}NH_{2}$, $-NHR^{7}NHR^{5}$, $-NHR^{7}O$, $-N(R^{5})R^{7}NH_{2}$, $-N(R^{5})R^{7}NHR^{5}$, $-N(R^{5})R^{7}O$, $-OR^{7}OH$, $-OR^{7}OR^{5}$, $-OR^{7}NH_{2}$, $-OR^{7}NHR^{5}$, $-OR^{7}O$, $-OC(O)R^{5}$, $-NHC(O)R^{5}$. $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, $-C(O)Q, -R^6C(O)H, -R^6C(O)R^5, -R^6C(O)OH, -R^6C(O)OR^5, -R^6C(O)NH_2$ $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, $-O(C(R^9)_2)_{q^7}$, $-S(O)_m(C(R^9)_2)_{q^7}$, $-NH(C(R^9)_2)_{q^7}$, $-NR^{10}(C(R^9)_2)_{q^7}$, $-(C(R^9)_2)_{q^7}$ $-(C(R^9)_2)_0O-$, $-(C(R^9)_2)_0S(O)_m-$, $-(C(R^9)_2)_0NH-$, $-(C(R^9)_2)_0NR^{10}-$, $-C\equiv C-$, cis and trans -CH=CH- and cycloalkyl of 3 to 10 carbon atoms; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO2, -NH2, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, $-NHR^5$, -Q, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6Q$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^{7}NHR^{5}$, $-NHR^{7}Q$, $-N(R^{5})R^{7}NH_{2}$, $-N(R^{5})R^{7}NHR^{5}$, $-N(R^{5})R^{7}Q$, $-OR^{7}OH$, $-R^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-R^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, -C(O)Q, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)O$, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, $-NHSO_2-, \quad -SO_2NH-, \quad -C(OH)H-, \quad -O(C(R^9)_2)_q^-, \quad -S(O)_m(C(R^9)_2)_q^-, \quad -NH(C(R^9)_2)_q^-,$ $-NR^{10}(C(R^9)_2)_{q^{-1}}, -(C(R^9)_2)_{q^{-1}}, -(C(R^9)_2)_{q^{-1}}O^{-1}, -(C(R$ -($C(R^9)_2$) $_qNR^{10}$ -, -C \equiv C-, cis and trans -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, $-S(O)_{m}R^{5}$, $-NHSO_{2}R^{5}$, $-R^{6}OH$, $-R^{6}OR^{5}$, $-R^{6}NH_{2}$, $-R^{6}NHR^{5}$, $-R^{6}Q$, $-R^{6}SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^{7}NHR^{5}$, $-NHR^{7}Q$, $-N(R^{5})R^{7}NH_{2}$, $-N(R^{5})R^{7}NHR^{5}$, $-N(R^{5})R^{7}Q$, $-QR^{7}QH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7O$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, -C(O)O, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)O$, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, $-NHSO_{2^{-}}, \quad -SO_{2}NH-, \quad -C(OH)H-, \quad -O(C(R^{9})_{2})_{q}^{-}, \quad -S(O)_{m}(C(R^{9})_{2})_{q}^{-}, \quad -NH(C(R^{9})_{2})_{q}, \quad -NH(C(R^{9})_{2})_{q}^{-}, \quad$ $-NR^{10}(C(R^9)_2)_q, \quad -(C(R^9)_2)_q{}^-, \quad -(C(R^9)_2)_qO-, \quad -(C(R^9)_2)_qS(O)_m{}^-, \quad -(C(R^9)_2)_qNH-, \quad -(C(R^9)_2)_q(R^9)_q -(C(R^9)_2)_qNH-, \quad -(C(R^9)_2)_q(R^9)_q -(C(R^9)_2)_q -(C(R^9)_$ $-(C(R^9)_2)_QNR^{10}$ -, $-C\equiv C$ -, cis and trans -CH=CH- and cycloalkyl of 3 to 10 carbon atoms; and a moiety of the formula

$$\begin{array}{c|c}
R^{1a} & R^{1b} \\
\hline
R^{1c} & R^{1c}
\end{array}$$

E is -NH-, $-NR^5$ -, -O-, $-S(O)_m$ -, -C(O)-, $-CH_2$ -, $-CHR^5$ - or $-CR^5R^5$ -;

Q is $-NR^5R^5$ and further provided that when each R^5 is independently selected from alkyl and alkenyl, R^5R^5 may optionally be taken together with the nitrogen atom to which they are attached forming a heterocyclyl ring of 3 to 8 atoms, optionally containing 1 or 2 additional heteroatoms which may be the same or different selected from N, O and S;

R^{1a}, R^{1b}, R^{1c}, R^{1d} and R^{1e} are each, independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, $-OR^5$, $-NHR^5$, -O, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^6OH$, $-R^6OR^5$, $-R^6NH_2$, $-R^6NHR^5$, $-R^6O$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7O$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, -C(O)Q, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$ $-R^{6}C(O)NHR^{5},\ -R^{6}C(O)Q,\ -R^{6}OC(O)R^{5},\ -R^{6}OC(O)NH_{2},\ -\ R^{6}OC(O)NHR^{5},\ -aryl,$ -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -R¹¹, -OR¹¹, -NHR¹¹ and -R⁶OC(O)O; R^{2a}, R^{2b}, and R^{2c}, are each, independently selected from -H, -aryl, -CH₂aryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-S(O)_mR^5$, $-NHSO_2R^5$, $-R^{11}$, $-OR^{11}$, $-R^6OH$, $-R^6OR^5$, $-R^6SH$, $-R^6S(O)_mR^5$, $-OR^7OH$, $-OR^7OR^5$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, -C(O)Q, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^{6}C(O)NHR^{5}$, $-R^{6}C(O)Q$, $-R^{6}OC(O)R^{5}$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, $-R^6OC(O)Q$, $-G-(C(R^9)_2)_p-R^{12}$, $-(C(R^9)_2)_q-R^{12}$.

G is -NH-, $-NR^{10}$ -, -O- or $-S(O)_m$ -;

 R^3 is selected from alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, -CHO, 1,3-dioxolane, $-NO_2$, -CN, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, -(C(

 $-(C(R^9)_2)_0 J$, $-(C(R^9)_2)_0 NH_2$, $-(C(R^9)_2)_t H$, $-G(C(R^9)_2)_0 OR^{10}$, $-G(C(R^9)_2)_0 R^{12}$, and $-G(C(R^9)_2)_DOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of $-R^{10}$, $-(C(R^9)_2)_5R^{12}$, -CHO, 1,3-dioxolane, $-NO_2$, -CN, $-CO_2H$, $-CONH_2$ $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_0OH$, $-(C(R^9)_2)_0OR^{10}$, $-(C(R^9)_2)_0NHR^{10}$, $-(C(R^9)_2)_g J$, $-(C(R^9)_2)_g NH_2$, $-(C(R^9)_2)_r H$, $-G(C(R^9)_2)_p OR^{10}$, $-G(C(R^9)_2)_p R^{12}$, and $-G(C(R^9)_2)_DOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_6R^{12}$. -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰. $-(C(R^9)_2)_0OH$, $-(C(R^9)_2)_0OR^{10}$, $-(C(R^9)_2)_0NHR^{10}$, $-(C(R^9)_2)_0J$, $-(C(R^9)_2)_0NH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S where the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_8R^{12}$, -CHO, 1.3-dioxolane, $-NO_2$, -CN, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_0OH$, $-(C(R^9)_2)_0OR^{10}$, $-(C(R^9)_2)_0NHR^{10}$, $-(C(R^9)_2)_0J$, $-(C(R^9)_2)_0NH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -R¹⁰, -(C(R⁹)₂)₈R¹², -CHO, 1,3-dioxolane, -NO₂, -CN, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_0OH$, $-(C(R^9)_2)_0OR^{10}$, $-(C(R^9)_2)_0NHR^{10}$, $-(C(R^9)_2)_0J$, $-(C(R^9)_2)_0NH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_0OR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$;

 R^4 is selected from -(C(R^9)₂)_rH, optionally substituted with one or more of - R^{10} , -(C(R^9)₂)_sR¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, -(C(R^9)₂)_qOH, -(C(R^9)₂)_qOR¹⁰, -(C(R^9)₂)_qNHR¹⁰, -(C(R^9)₂)_qJ, -(C(R^9)₂)_qNH₂, -(C(R^9)₂)_rH, -G(C(R^9)₂)_pOR¹⁰, -G(C(R^9)₂)_pR¹², and -G(C(R^9)₂)_pOH; alkenyl of 2 to 6 carbon atoms, optionally substituted with one or more of - R^{10} ,

-(C(R⁹)₂)₈R¹²,-CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qJ$, $-(C(R^9)_2)_0NH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_0OR^{10}$, $-G(C(R^9)_2)_nR^{12}$, and $-G(C(R^9)_2)_nOH$; alkynyl of 2 to 6 carbon atoms, optionally substituted with one or more of -R¹⁰, -(C(R⁹)₂)₂R¹², -CHO, 1,3-dioxolane, -NO₂, -CN, -CO₂H, -CONH₂ -CO₂R¹⁰. $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_aOH$, $-(C(R^9)_2)_aOR^{10}$, $-(C(R^9)_2)_aNHR^{10}$, $-(C(R^9)_2)_aJ$, $-(C(R^9)_2)_0NH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_0OR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, -CHO, 1,3dioxolane, -NO₂, -CN, -CO₂H, -CONH₂, -CO₂R¹⁰, -CONHR¹⁰, -COR¹⁰, $-(C(R^9)_2)_0OH$, $-(C(R^9)_2)_0OR^{10}$, $-(C(R^9)_2)_0NHR^{10}$, $-(C(R^9)_2)_0J$, $(C(R^9)_2)_0NH_2$. $-(C(R^9)_2)_pH$, $-G(C(R^9)_2)_pOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, -CHO, 1,3-dioxolane, $-NO_2$, -CN, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_0OH$, $-(C(R^9)_2)_0OR^{10}$, $-(C(R^9)_2)_0NHR^{10}$, $-(C(R^9)_2)_0J$, $-(C(R^9)_2)_0NH_2$, $-(C(R^9)_2)_rH$, $-G(C(R^9)_2)_nOR^{10}$, $-G(C(R^9)_2)_pR^{12}$, and $-G(C(R^9)_2)_pOH$; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from $-R^{10}$, $-(C(R^9)_2)_s R^{12}$, -CHO, 1,3-dioxolane, $-NO_2$, -CN, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_aOH$, $-(C(R^9)_2)_aOR^{10}$, $-(C(R^9)_2)_aNHR^{10}$, $-(C(R^9)_2)_aJ$, $-(C(R^9)_2)_{a}NH_2, -(C(R^9)_2)_{r}H, -G(C(R^9)_2)_{p}OR^{10}, -G(C(R^9)_2)_{p}R^{12}, \text{ and } -G(C(R^9)_2)_{p}OH;$ R⁵ is a monovalent group independently selected from alkyl of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms:

R⁶ is a divalent group selected from alkyl of 1 to 6 carbon atoms, alkenyl of 2 to 6 carbon atoms, and alkynyl of 2 to 6 carbon atoms;

R⁷ is a divalent alkyl group of 2 to 6 carbon atoms;

R⁸ is a cycloalkyl ring of 3 to 10 carbon atoms that may optionally be substituted with one or more alkyl groups of 1 to 6 carbon atoms; aryl of 6 to 12 carbon atoms optionally substituted with 1 to 4 substituents which may be the same or different selected from -H,-aryl, -CH2aryl, -NHaryl, -Oaryl, -S(O)maryl, -J, -NO2, -NH2, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, $-NHR^{5}$, -O, $-S(O)_{m}R^{5}$, $-NHSO_{2}R^{5}$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^{6}OH$, $-R^{6}OR^{5}$, $-R^{6}NH_{2}$, $-R^6NHR^5$, $-R^6O$, $-R^6SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7O$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, -C(O)Q, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6R^{12}$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, -R⁶OC(O)NHR⁵ and -R⁶OC(O)O; a heteroaryl ring having 5 or 6 atoms containing 1 to 4 heteroatoms or particularly 1 or 2 heteroatoms which may be the same or different, selected from N, O and S wherein the heteroaryl ring may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H. -arvl, -CH₂aryl, -NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, $-S(O)_{m}R^{5}$, $-NHSO_{2}R^{5}$, $-R^{11}$, $-OR^{11}$, $-NHR^{11}$, $-R^{6}OH$, $-R^{6}OR^{5}$, $-R^{6}NH_{2}$, $-R^{6}NHR^{5}$, $-R^{6}Q, -R^{6}SH, -R^{6}S(O)_{m}R^{5}, -NHR^{7}OH, -NHR^{7}OR^{5}, -N(R^{5})R^{7}OH, -N(R^{5})R^{7}OR^{5}, -N(R^{5})R^{7}OR^{5},$ $-NHR^7NH_2$, $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^6C(O)R^5$, $-NHR^6C(O)R^5$, $-C(O)R^5$, $-C(O)OR^5$, $-C(O)NHR^5$, -C(O)O, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6R^{12}$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$ and -R⁶OC(O)Q; a bicyclic heteroaryl ring system having 8 to 20 atoms containing 1 to 4 heteroatoms which may be the same or different selected from N, O and S wherein the bicyclic heteroaryl ring system may be optionally substituted with 1 to 4 substituents which may be the same or different selected from -H, -aryl, -CH2aryl,

17

-NHaryl, -Oaryl, -S(O)_maryl, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R¹¹, -OR¹¹, -NHR¹¹, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶R¹², -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)NH₂, -R⁶C(O)NH₂, -R⁶C(O)OR⁵, -R⁶C(O)

 R^9 is independently -H, -F or - R^5 ;

R¹⁰ is an alkyl group of 1 to 12 carbon atoms, preferred is 1 to 6 carbon atoms;

R¹¹ is a cycloalkyl group of 3 to 10 carbon atoms;

 R^{12} is $-N(O)_n R^{13} R^{14}$ or $-N^+ (R^{10} R^{13} R^{14}) J^-$; provided that when R^{12} is $N(O)_n R^{13} R^{14}$ and n is 1, R^{13} or R^{14} are not H;

 R^{13} and R^{14} are independently selected from a group consisting of -H, -R⁵, -R¹¹, -(C(R⁹)₂)_qaryl-R¹⁵, -(C(R⁹)₂)_qheteroaryl-R¹⁵, -(C(R⁹)₂)_pheterocyclyl-R¹⁵, -(C(R⁹)₂)_pOR¹⁶, -(C(R⁹)₂)_pNR¹⁶R¹⁷, -(C(R⁹)₂)_pS(O)_mR¹⁶, -(C(R⁹)₂)_pCO₂R¹⁶, -(C(R⁹)₂)_pC(O)NHR¹⁶ and -(C(R⁹)₂)_pC(O)R¹⁵; further provided that R¹³ and R¹⁴ may optionally be taken together with the nitrogen to which they are attached forming a heterocyclyl, heteroaryl or bicyclyl heteroaryl ring optionally substituted on either nitrogen or carbon by one or more selected from the group, -R⁵, -R¹¹, -(C(R⁹)₂)_qarylR¹⁵, -(C(R⁹)₂)_qheteroarylR¹⁵, -(C(R⁹)₂)_qheterocyclylR¹⁵, -(C(R⁹)₂)_qCO₂R¹⁶,-(C(R⁹)₂)_qC(O)NHR¹⁶, and -(C(R⁹)₂)_qC(O)R¹⁵; or optionally substituted on carbon by -F, -(C(R⁷)₂)_qOR¹⁶, -(C(R⁷)₂)_qNR¹⁶R¹⁷, and

18

 $-(C(R^9)_2)_q S(O)_m R^{16}; \ or \ optionally \ substituted \ on \ nitrogen \ by \ -(C(R^9)_2)_p OR^{16}, \\ -(C(R^9)_2)_p NR^{16} R^{17}, \ and \ -(C(R^9)_2)_p S(O)_m R^{16};$

 R^{15} is independently selected from a group consisting of -H, -R⁵, -R¹¹, -(C(R⁹)₂)_qaryl,

 $-(C(R^9)_2)_q$ heteroaryl, $-(C(R^9)_2)_q$ heterocyclyl, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$,

 $-(C(R^9)_2)_aNH_2$, $-(C(R^9)_2)_aNHR^{10}$, $-(C(R^9)_2)_aR^{10}$, $-(C(R^9)_2)_aS(O)_mR^{10}$,

 $-(C(R^9)_2)_qCO_2R^{10}, \ -(C(R^9)_2)_qCONHR^{10}, \ -(C(R^9)_2)_qCONR^{10}R^{10}, \ -(C(R^9)_2)_qCOR^{10}, \ -(C(R^9)$

 $(C(R^9)_2)_qCO_2H$, and $-(C(R^9)_2)_qCONH_2$;

$$\begin{split} R^{16} \text{ and } R^{17} \text{ are independently selected from a group consisting of } -H, -R^5, -R^{11}, \\ -(C(R^9)_2)_q \text{aryl}, & -(C(R^9)_2)_q \text{heteroaryl}, & -(C(R^9)_2)_q \text{heterocyclyl}, & -(C(R^9)_2)_p \text{OH}, \\ -(C(R^9)_2)_p \text{OR}^{10}, & -(C(R^9)_2)_p \text{NH}_2, & -(C(R^9)_2)_p \text{NHR}^{10}, & -(C(R^9)_2)_p \text{NR}^{10} R^{10}, \\ -(C(R^9)_2)_p \text{S}(O)_m R^{10}, -(C(R^9)_2)_p \text{CO}_2 R^{10}, -(C(R^9)_2)_p \text{CONHR}^{10}, & -(C(R^9)_2)_p \text{CONH}^{10} R^{10}, \\ -(C(R^9)_2)_p \text{COR}^{10}, -(C(R^9)_2)_p \text{CO}_2 H, \text{ and } -(C(R^9)_2)_p \text{CONH}_2; \end{split}$$

 R^{18} is independently selected from the group consisting of -H, -aryl, -R⁵, -R⁶NH₂, -R⁶NHR⁵ and -R⁶O;

provided that, when T and Z are carbon, A is absent, r is 0 and R^4 is $-(C(R^9)_2)_rH$, then,

- a. R³ is not unsubstituted thiophene, furan, thiazole, imidazole,
 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyridine, phenyl, alkenyl or
 alkynyl; or
- b. R^3 is not monosubstituted by $-R^{10}$, $-(C(R^9)_2)_qOH$, or $-(C(R^9)_2)_qOR^{10}$ when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and
- c. R^{13} and R^{14} are not alkyl of 1 to 6 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine when R^3 is substituted by $-(C(R^9)_2)_s R^{12}$ and R^{12} is $-NR^{13}R^{14}$;

19

further provided that, when T and Z are carbon, A is absent and R⁴ is phenyl, then,

- a. R^4 is not substituted by $-NO_2$, -CN, $-CO_2H$, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^7)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qNH_2$ or unsubstituted when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine; and
- b. R^{13} and R^{14} are not independently alkyl of 1 to 3 carbon atoms when R^3 is thiophene, furan, thiazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole or pyridine, wherein R^4 is substituted by $-(C(R^9)_2)_sR^{12}$ and s is 0 and R^{12} is $-NR^{13}R^{14}$;

additionally provided that, when T and Z are carbon, then,

- a. carbon-8 is not substituted by -OH, -OR¹⁰, -SR¹⁰, or -OR¹¹ when carbon-5 is substituted by an imidazole, oxazole or thiazole ring that is fused to a 6-membered aryl or heteroaryl ring having 0 to 2 nitrogen atoms and wherein the fused bicyclic heteroaryl ring is attached to carbon-5 of Formula (I) via carbon-2 of the imidazole, oxazole or thiazole ring; and
- b. carbon-8 is not substituted by -OH, -OR 10 , -SR 10 , or -OR 11 when X is -O- and carbon-5 is substituted by aryl or heteroaryl;

further provided that when either T or Z are N, then R^{2c} is absent; or a pharmaceutically acceptable salt thereof.

Among the preferred groups of compounds of Formula (I) of this invention including pharmaceutically acceptable salts thereof are those in the subgroups

20

below, wherein the other variables of Formula (I) in the subgroups are as defined above wherein:

- a) $X \text{ is } -NH^{-}, -NR^{5} \text{ and } -O^{-};$
- b) T and Z are carbon;
- c) T is N and Z is carbon;
- d) T is carbon and Z is N;
- e) T and Z are carbon, n is 0 and X is -NH-;
- f) T is carbon and Z is N, n is 0 and X is –NH-;
- g) T is N and Z is carbon, n is 0 and X is -NH-;
- h) T and Z are carbon, n is 0, X is -NH- and R¹ is aryl;
- i) T is carbon and Z is N, n is 0, X is -NH- and R^1 is aryl;
- j) T is N and Z is carbon, n is 0, X is -NH- and R¹ is aryl;

Among the additionally preferred groups of compounds of Formula (I) of this invention including pharmaceutically acceptable salts thereof are those in the subgroups below, wherein the other variables of Formula (I) in the subgroups are as defined above wherein:

a) 3-cyanoquinolines, 3-cyano-1,6-naphthyridines and 3-cyano-1,7-naphthyridines of Formula (I) wherein:

X is -NH-;

n is 0;

 R^1 is a phenyl ring optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂,

21

-NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)OH, -R⁶C(O)NH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)q₋, -S(O)_m(C(R⁹)₂)q₋, -NH(C(R⁹)₂)q, -NR¹⁰(C(R⁹)₂)q, -(C(R⁹)₂)q⁻, -(C(R⁹)₂)qO-, -(C(R⁹)₂)qS(O)_m-, -(C(R⁹)₂)qNH-, -(C(R⁹)₂)qNR¹⁰-, -C \equiv C-, cis and trans -CH=CH- and cycloalkyl of 3 to 10 carbon atoms; or a pharmaceutically acceptable salt thereof.

b) 3-cyanoquinolines, of Formula (I) wherein:

T and Z are carbon;

X is -NH-;

n is 0;

R¹ is a phenyl ring optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)NH₂, -R⁶C(O)NH₂, -R⁶C(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -NHC(O)-, -C(O)NH₂, -C(O)NH

22

- $(C(R^9)_2)_qS(O)_{m^-}$, - $(C(R^9)_2)_qNH^-$, - $(C(R^9)_2)_qNR^{10}$ -, - $C\equiv C$ -, *cis* and *trans* -CH=CH- and cycloalkyl of 3 to 10 carbon atoms; or a pharmaceutically acceptable salt thereof.

c) 3-cyanoquinolines, 3-cyano-1,6-naphthyridines and 3-cyano-1,7-naphthyridines of Formula (I) wherein:

X is -NH-;

n is 0;

A is absent;

R¹ is a phenyl ring optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q $-S(O)_{m}R^{5}$, $-NHSO_{2}R^{5}$, $-R^{6}OH$, $-R^{6}OR^{5}$, $-R^{6}NH_{2}$, $-R^{6}NHR^{5}$, $-R^{6}O$, $-R^{6}SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^{7}NHR^{5}$, $-NHR^{7}Q$, $-N(R^{5})R^{7}NH_{2}$, $-N(R^{5})R^{7}NHR^{5}$, $-N(R^{5})R^{7}Q$, $-OR^{7}OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7Q$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^{6}C(O)R^{5}$, $-NHR^{6}C(O)R^{5}$, $-C(O)R^{5}$, $-C(O)OR^{5}$, $-C(O)NHR^{5}$, -C(O)O, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, $-R^6OC(O)Q$ and YR^8 groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -NHC(O)-, $-NHSO_2$ -, $-SO_2NH$ -, -C(OH)H-, $-O(C(R^9)_2)_{OH}$ -C(O)NH-, $-S(O)_m(C(R^9)_2)_{Q^-}$, $-NH(C(R^9)_2)_Q$, $-NR^{10}(C(R^9)_2)_Q$, $-(C(R^9)_2)_Q^-$, $-(C(R^9)_2)_Q^-$ and cycloalkyl of 3 to 10 carbon atoms;

or a pharmaceutically acceptable salt thereof.

23

d) 3-cyanoquinolines of Formula (I) wherein:

X is -NH-;

T and Z are carbon;

n is 0;

A is absent;

 R^1 is a phenyl ring optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -C(O)Q, -R⁶C(O)R⁵, -NHC⁶C(O)R⁵, -C(O)OR⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)Q, -R⁶C(O)NH₂, -R⁶C(O)NH₂, -R⁶C(O)NH₂, -R⁶C(O)Q, -R⁶C(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -NHC(O)-, -C(O)NH₂, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_Q-, -S(O)_m(C(R⁹)₂)_Q-, -NH(C(R⁹)₂)_Q-, -NR¹⁰(C(R⁹)₂)_Q-, -C(C(R⁹)₂)_Q-, -C(C(R⁹)₂)_Q

e) 3-cyanoquinolines of Formula (I) wherein:

or a pharmaceutically acceptable salt thereof.

T and Z are carbon;

X is -NH-;

n is 0;

R¹ is a phenyl ring substituted with 1 to 4 substituents which may be the same or different independently selected from H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q,

24

 $-S(O)_{m}R^{5}, -NHSO_{2}R^{5}, -R^{6}OH, -R^{6}OR^{5}, -R^{6}NH_{2}, -R^{6}NHR^{5}, -R^{6}Q, -R^{6}SH, -R^{6}S(O)_{m}R^{5}, -NHR^{7}OH, -NHR^{7}OR^{5}, -N(R^{5})R^{7}OH, -N(R^{5})R^{7}OR^{5}, -NHR^{7}NH_{2}, -NHR^{7}NHR^{5}, -NHR^{7}Q, -N(R^{5})R^{7}NH_{2}, -N(R^{5})R^{7}NHR^{5}, -N(R^{5})R^{7}Q, -OR^{7}OH, -OR^{7}OR^{5}, -OR^{7}NH_{2}, -OR^{7}NHR^{5}, -OR^{7}Q, -OC(O)R^{5}, -NHC(O)R^{5}, -NHC(O)NHR^{5}, -OR^{6}C(O)R^{5}, -NHR^{6}C(O)R^{5}, -C(O)R^{5}, -C(O)OR^{5}, -C(O)NHR^{5}, -C(O)Q, -R^{6}C(O)H, -R^{6}C(O)R^{5}, -R^{6}C(O)OH, -R^{6}C(O)NH_{2}, -R^{6}C(O)NH_{2}, -R^{6}C(O)Q, -R^{6}C(O)R^{5}, -R^{6}OC(O)NH_{2}, -R^{6}OC(O)NHR^{5}, -R^{6}OC(O)Q, -C(O)NH_{2}, -NHC(O)-, -NHSO_{2}, -SO_{2}NH-, -C(OH)H-, -O(C(R^{9})_{2})q^{-}, -S(O)_{m}(C(R^{9})_{2})q^{-}, -NH(C(R^{9})_{2})q^{-}, -NR^{10}(C(R^{9})_{2})q^{-}, -(C(R^{9})_{2})q^{-}, -(C(R^{9})_{2})q$

A is absent;

 R^4 is $(C(R^9)_2)_rH$;

r is 0;

or a pharmaceutically acceptable salt thereof.

Among the broadly preferred groups of compounds of Formula (I) of this invention including pharmaceutically acceptable salts thereof are those in the subgroups below, wherein the other variables of Formula (I) in the subgroups are as defined above wherein:

a) 3-cyanoquinolines of Formula (I) wherein:

T and Z are carbon;

R^{2a} and R^{2b} are hydrogen;

 R^{2c} is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵;

X is -NH-;

n is 0;

R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃,

25

-COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -NHR⁷NHR⁵, -NHR⁷Q, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)OR⁵, -C(O)OR⁵, -C(O)OH₂, -R⁶C(O)NHR⁵, -R⁶C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)NH₂, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C≡C-, cis and trans -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

or a pharmaceutically acceptable salt thereof.

b) 3-cyanoquinolines of Formula (I) wherein:

T and Z are carbon;

R^{2a} and R^{2b} are hydrogen;

 R^{2c} is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵;

X is -NH-;

n is 0;

 R^1 is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -NHR⁷NH₂, -NHR⁷NH₂, -NHR⁷NH₂, -OR⁷NH₂, -OR⁷NH₂, -OR⁷OH, -OR⁷OR⁵, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NH₂, -OR⁷NH₂, -OR⁷NH₂, -OR⁷OH, -NHC(O)R⁵, -NHC(O)NHR⁵,

26

 $-OR^6C(O)R^5, -NHR^6C(O)R^5, -C(O)R^5, -C(O)OR^5, -C(O)NHR^5, -C(O)Q, \\ -R^6C(O)H, -R^6C(O)R^5, -R^6C(O)OH, -R^6C(O)OR^5, -R^6C(O)NH_2, -R^6C(O)NH_2, \\ -R^6C(O)Q, -R^6OC(O)R^5, -R^6OC(O)NH_2, -R^6OC(O)NHR^5, -R^6OC(O)Q and YR^8 \\ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, \\ -C(O)NH-, -NHC(O)-, -NHSO_2-, -SO_2NH-, -C(OH)H-, -O(C(R^9)_2)_q-, \\ -S(O)_m(C(R^9)_2)_q-, -NH(C(R^9)_2)_q^-, -NR^{10}(C(R^9)_2)_q^-, -(C(R^9)_2)_q^-, -(C(R^$

A is absent;

or a pharmaceutically acceptable salt thereof.

c) 3-cyanoquinolines of Formula (I) wherein:

T and Z are carbon;

R^{2a} and R^{2b} are hydrogen;

 R^{2c} is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵;

X is -NH-;

n is 0;

R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)OH, -R⁶C(O)OH, -R

27

-C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -S(O)_m(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C \equiv C-, cis and trans -CH=CH-and cycloalkyl of 3 to 10 carbon atoms;

 R^4 is $-(C(R^9)_2)_rH$:

r is 0:

A is absent;

 R^3 is attached to carbon-7 of Formula (I) and is selected from aryl, heteroaryl, bicyclic heteroaryl, alkenyl, alkynyl wherein each aryl, heteroaryl, bicyclic heteroaryl, alkenyl, and alkynyl is optionally substituted by one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, -CHO, 1,3-dioxolane, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOR^{10}$, $-(C(R^9)_2)_qNHR^{10}$, $-(C(R^9)_2)_qNH_2$, $G(C(R^9)_2)_pOR^{10}$, $G(C(R^9)_2)_pOH$, and $G(C(R^9)_2)_pR^{12}$;

or a pharmaceutically acceptable salt thereof.

d) 3-cyanoquinolines of Formula (I) wherein:

T and Z are carbon;

 R^{2a} and R^{2b} are hydrogen;

 R^{2c} is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵;

X is -NH-;

n is 0;

R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q,

28

 $-R^{6}C(O)H, -R^{6}C(O)R^{5}, -R^{6}C(O)OH, -R^{6}C(O)OR^{5}, -R^{6}C(O)NH_{2}, -R^{6}C(O)Q and YR^{8} groups wherein Y is independently selected from -C(O)-, -C(O)O-, -C(O)O-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R^{9})₂)_Q⁻, -C(C(R^{9})₂)_Q⁻, -C(C(R^{9})₂)_Q⁻, -C(C(R^{9})₂)_Q⁻, -C(C(R^{9})₂)_QO-, -C(C(R^{9})₂)_QNH-, -C(C(R^{9})₂)_QNH-, -C(C(R^{9})₂)_QNR¹⁰-, -C(C(R^{9})₂)_QNH-, -C(C(R^{9})₂)_QNR¹⁰-, -C(C(R^{9})₂)_QNR¹⁰-, -C(C(R^{9})₂)_QNH-, -C(C(R^{9})₂)_QNR¹⁰-, -C(C(R^{9})₂)_QNR¹⁰-, -C(C(R^{9})₂)_QNH-, -C(C(R^{9})₂)_QNR¹⁰-, -C(C(R^{9})_QNR¹⁰-, -C(C(R^{9})_QNR¹⁰-, -C(C(R^{9})_QNR¹⁰-, -C(C(R^{9})_QNR¹⁰-, -C(C(R^{9})_QNR¹⁰-, -C(C(R^{9})_QNR¹⁰-, -C(C(R^{$

$$R^4$$
 is $-(C(R^9)_2)_rH$;

r is 0;

A is absent;

 R^3 is attached to carbon-6 of Formula (I) and is selected from aryl, heteroaryl, bicyclic heteroaryl, alkenyl, alkynyl wherein each aryl, heteroaryl, bicyclic heteroaryl, alkenyl, and alkynyl is optionally substituted by one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, -CHO, 1,3-dioxolane, $-CONH_2$, $-CO_2R^{10}$, $-CONHR^{10}$, $-COR^{10}$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_qOH$, $-(C(R^9)_2)_pOH^{10}$, $-(C(R^9)_2)_pOH$, and $-(C(R^9)_2)_pOH$, and -(C

or a pharmaceutically acceptable salt thereof.

Among the more preferred groups of compounds of Formula (I) of this invention including pharmaceutically acceptable salts thereof are those in the subgroups below wherein the other variables of Formula (I) in the subgroups are as defined above wherein:

a) 3-cyanoquinolines of Formula (I) wherein:

T and Z are carbon;

R^{2a} and R^{2b} are hydrogen;

 R^{2c} is attached to carbon-6 or carbon-7 of Formula (I) and is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵; X is -NH-:

n is 0;

R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, $-S(O)_{m}R^{5}$, $-NHSO_{2}R^{5}$, $-R^{6}OH$, $-R^{6}OR^{5}$, $-R^{6}NH_{2}$, $-R^{6}NHR^{5}$, $-R^{6}O$, $-R^{6}SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$, $-NHR^{7}NHR^{5}$, $-NHR^{7}Q$, $-N(R^{5})R^{7}NH_{2}$, $-N(R^{5})R^{7}NHR^{5}$, $-N(R^{5})R^{7}Q$, $-QR^{7}QH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7O$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$. $-OR^{6}C(O)R^{5}$, $-NHR^{6}C(O)R^{5}$, $-C(O)R^{5}$, $-C(O)OR^{5}$, $-C(O)NHR^{5}$, -C(O)Q, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NHR^5$, $-R^6C(O)Q$, $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, $-R^6OC(O)Q$ and $-YR^8$ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(\mathbb{R}^9)₂)₀-, -C(O)NH-. $-S(O)_m(C(R^9)_2)_{q^-}, \quad -NH(C(R^9)_2)_{q^-}, \quad -NR^{10}(C(R^9)_2)_{q^-}, \quad -(C(R^9)_2)_{q^-}, \quad -(C(R^9)_2)_{$ $-(C(R^9)_2)_0S(O)_{m^-}$, $-(C(R^9)_2)_0NH^-$, $-(C(R^9)_2)_0NR^{10}$ -, -C=C-, cis and trans -CH=CHand cycloalkyl of 3 to 10 carbon atoms;

 R^4 is $-(C(R^9)_2)_rH$;

r is 0;

A is absent;

 R^3 is attached to carbon-6 or carbon-7 of Formula (I) and is selected from aryl, heteroaryl, bicyclic heteroaryl, alkenyl, alkynyl wherein each aryl, heteroaryl, bicyclic heteroaryl, alkenyl, alkynyl is optionally substituted by one or more of $-R^{10}$, $-(C(R^9)_2)_sR^{12}$, -CHO, and 1, 3-dioxolane; or a pharmaceutically acceptable salt thereof.

b) 3-cyanoquinolines of Formula (I) wherein:

T and Z are carbon:

X is -NH-;

n is 0;

30

R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)OR⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)NH₂, -R⁶C(O)NH₂, -R⁶C(O)NH₃, -R⁶C(O)Q, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NH₃, -R⁶OC(O)Q, -OC(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -C(C(P⁹)₂)_q-, -C(C(P⁹)₂)_q-, -C(C(P⁹)₂)_q-, -C(C(R⁹)₂)_q-, -

 R^{2a} and R^{2b} are H;

 R^{2c} is attached to carbon-6 and is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵;

 R^3 is attached to carbon–7 of Formula (I) and is selected from heteroaryl, phenyl, alkenyl of 2 to 6 carbon atoms or alkynyl of 2 to 6 carbon atoms with each heteroaryl, phenyl, alkenyl and alkynyl group further substituted by one or more of the group - $(C(R^9)_2)_sR^{12}$;

A is absent;

$$R^4$$
 is $(C(R^9)_2)_rH$;

r is 0;

or a pharmaceutically acceptable salt thereof.

c) 3-cyanoquinolines of Formula (I) wherein:

T and Z are carbon;

X is -NH-;

31

n is 0;

R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q, -S(O)_mR⁵, -NHSO₂R⁵, -R⁶OH, -R⁶OR⁵, -R⁶NH₂, -R⁶NHR⁵, -R⁶Q, -R⁶SH, -R⁶S(O)_mR⁵, -NHR⁷OH, -NHR⁷OR⁵, -N(R⁵)R⁷OH, -N(R⁵)R⁷OR⁵, -NHR⁷NH₂, -NHR⁷NH₂, -N(R⁵)R⁷NH₂, -N(R⁵)R⁷NHR⁵, -N(R⁵)R⁷Q, -OR⁷OH, -OR⁷OR⁵, -OR⁷NH₂, -OR⁷NHR⁵, -OR⁷Q, -OC(O)R⁵, -NHC(O)R⁵, -NHC(O)NHR⁵, -OR⁶C(O)R⁵, -NHR⁶C(O)R⁵, -C(O)R⁵, -C(O)OR⁵, -C(O)NHR⁵, -C(O)Q, -R⁶C(O)H, -R⁶C(O)R⁵, -R⁶C(O)OH, -R⁶C(O)NH₂, -R⁶C(O)NH₂, -R⁶C(O)Q and -YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, -NHSO₂-, -SO₂NH-, -C(OH)H-, -O(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -NH(C(R⁹)₂)_q-, -NR¹⁰(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -(C(R⁹)₂)_q-, -C(C(R⁹)₂)_qO-, -(C(R⁹)₂)_qS(O)_m-, -(C(R⁹)₂)_qNH-, -(C(R⁹)₂)_qNR¹⁰-, -C=C-, cis and trans -CH=CH- and cycloalkyl of 3 to 10 carbon atoms;

 R^{2a} and R^{2b} are H;

 R^{2c} is attached to carbon-7 of Formula (I) and is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵;

 R^3 is attached to carbon-6 of Formula (I) and is selected from heteroaryl, phenyl, alkenyl of 2 to 6 carbon atoms or alkynyl of 2 to 6 carbon atoms with each heteroaryl, phenyl, alkenyl and alkynyl group substituted by one or more of the group - $(C(R^9)_2)_s R^{12}$;

A is absent:

$$R^4$$
 is $-(C(R^9)_2)_rH$;

r is 0;

or a pharmaceutically acceptable salt thereof.

d) 3-cyanoquinolines of Formula (I) wherein:

X is -NH-:

WO 01/72711

32

```
T and Z are carbon;
```

n is 0;

 R^{2a} and R^{2b} are H;

 R^{2c} is attached to carbon–6- or carbon–7 of Formula (I) and is selected from -H, -J, -CF₃, -OCF₃, -R⁵, -OR⁵, -OR¹¹, -OR⁷OH, -OR⁷OR⁵ and -S(O)_mR⁵;

R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃,

-COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -Q,

 $-S(O)_{m}R^{5}$, $-NHSO_{2}R^{5}$, $-R^{6}OH$, $-R^{6}OR^{5}$, $-R^{6}NH_{2}$, $-R^{6}NHR^{5}$, $-R^{6}Q$, $-R^{6}SH$,

 $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$,

 $-NHR^7NHR^5$, $-NHR^7Q$, $-N(R^5)R^7NH_2$, $-N(R^5)R^7NHR^5$, $-N(R^5)R^7Q$, $-OR^7OH$,

 $-OR^7OR^5, -OR^7NH_2, -OR^7NHR^5 - OR^7Q, -OC(O)R^5, -NHC(O)R^5, -NHC(O)NHR^5, \\$

 $-OR^{6}C(O)R^{5}, -NHR^{6}C(O)R^{5}, -C(O)R^{5}, -C(O)OR^{5}, -C(O)NHR^{5}, -C(O)Q, -R^{6}C(O)H, -C(O)Q, -R^{6}C(O)R^{5}, -C(O)Q, -C(O)Q, -C(O)Q, -C(O)Q, -C(O)Q, -C(O)Q,$

 $-{}^{6}C(O)R^{5}$, $-R^{6}C(O)OH$, $-R^{6}C(O)OR^{5}$, $-R^{6}C(O)NH_{2}$, $-R^{6}C(O)NHR^{5}$, $-R^{6}C(O)Q$,

 $-R^6OC(O)R^5$, $-R^6OC(O)NH_2$, $-R^6OC(O)NHR^5$, $-R^6OC(O)Q$ and $-YR^8$ groups

wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-,

 $-NHC(O)-, -NHSO_2-, -SO_2NH-, -C(OH)H-, -O(C(R^9)_2)_q^{-}, -S(O)_m(C(R^9)_2)_q^{-}, \\$

 $-NH(C(R^9)_2)_{q^7}, -NR^{10}(C(R^9)_2)_{q^7}, -(C(R^9)_2)_{q^7}, -($

- $(C(R^9)_2)_qNH$ -, - $(C(R^9)_2)_qNR^{10}$ -, -C=C-, cis- and trans- -CH=CH- and cycloalkyl of

3 to 10 carbon atoms;

R³ is attached to carbon-6 or carbon-7 of Formula (I) and is alkenyl of 2 carbon atoms;

A is absent;

or a pharmaceutically acceptable salt thereof.

e) 3-cyanoquinolines of Formula (I) wherein:

X is -NH-;

T and Z are carbon;

n is 0;

 R^{2a} and R^{2b} are H;

R^{2c} is attached to carbon-6 or carbon-7 of Formula (I) and is selected from -H, -J, $-CF_3$, $-OCF_3$, $-R^5$, $-OR^5$, $-OR^{11}$, $-OR^7OH$, $-OR^7OR^5$ and $-S(O)_mR^5$; R¹ is phenyl optionally substituted with 1 to 4 substituents which may be the same or different independently selected from -H, -J, -NO₂, -NH₂, -OH, -SH, -CN, -N₃, -COOH, -CONH₂, -NHC(O)NH₂, -C(O)H, -CF₃, -OCF₃, -R⁵, -OR⁵, -NHR⁵, -O, $-S(O)_{m}R^{5}$, $-NHSO_{2}R^{5}$, $-R^{6}OH$, $-R^{6}OR^{5}$, $-R^{6}NH_{2}$, $-R^{6}NHR^{5}$, $-R^{6}Q$, $-R^{6}SH$, $-R^6S(O)_mR^5$, $-NHR^7OH$, $-NHR^7OR^5$, $-N(R^5)R^7OH$, $-N(R^5)R^7OR^5$, $-NHR^7NH_2$. $-NHR^{7}NHR^{5}$ $-NHR^{7}Q$, $-N(R^{5})R^{7}NH_{2}$, $-N(R^{5})R^{7}NHR^{5}$, $-N(R^{5})R^{7}Q$, $-OR^{7}OH$, $-OR^7OR^5$, $-OR^7NH_2$, $-OR^7NHR^5$, $-OR^7O$, $-OC(O)R^5$, $-NHC(O)R^5$, $-NHC(O)NHR^5$, $-OR^{6}C(O)R^{5}$, $-NHR^{6}C(O)R^{5}$, $-C(O)R^{5}$, $-C(O)OR^{5}$, $-C(O)NHR^{5}$, -C(O)Q, $-R^6C(O)H$, $-R^6C(O)R^5$, $-R^6C(O)OH$, $-R^6C(O)OR^5$, $-R^6C(O)NH_2$, $-R^6C(O)NH_2$ -R⁶C(O)O, -R⁶OC(O)R⁵, -R⁶OC(O)NH₂, -R⁶OC(O)NHR⁵, -R⁶OC(O)Q and YR⁸ groups wherein Y is independently selected from -C(O)-, -C(O)O-, -OC(O)-, -C(O)NH-, -NHC(O)-, $-NHSO_2-$, $-SO_2NH-$, -C(OH)H-, $-O(C(R^9)_2)_{G-}$, $-S(O)_m(C(R^9)_2)q^{\text{-}}, -NH(C(R^9)_2)q^{\text{-}}, -NR^{10}(C(R^9)_2)q^{\text{-}}, -(C(R^9)_2)q^{\text{-}}, -(C(R^9)_2)q^$ $-(C(R^9)_2)_{q}S(O)_{m}$ -, $-(C(R^9)_2)_{q}NH$ -, $-(C(R^9)_2)_{q}NR^{10}$ -, $-C\equiv C$ -, cis and trans -CH=CHand cycloalkyl of 3 to 10 carbon atoms; R³ is attached to carbon-6 or carbon-7 of Formula (I) and is alkynyl of 2 carbon

A is absent;

atoms;

or a pharmaceutically acceptable salt thereof.

Preferred compounds of the invention or a pharmaceutically acceptable salt thereof are:

4-(4-Chloro-2-fluoroanilino)-7-[5-(4-morpholinylmethyl)-3-thienyl]-3- quinoline-carbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[(E)-2-(4-pyridinyl)ethenyl]-3-quinoline-carbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[(E)-2-(2-pyridinyl)ethenyl]-3-quinoline-carbonitrile,

4-(2,4-Dichloroanilino)-7-[(E)-2-(4-pyridinyl)ethenyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(1,3-dioxolan-2-yl)-2-furyl]-3-quinoline-carbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(5-formyl-2-furyl)-3-quinolinecarbonitrile,

7-[5-(4-Morpholinylmethyl)-3-thienyl]-4-(4-phenoxyanilino)-3-quinolinecarbonitrile,

4-(4-Benzylanilino)-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloroanilino)-7-{5-[2-(4-morpholinyl)ethyl]-2-thienyl}-3-quinoline-carbonitrile,

4-(2,4-Dichloroanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloroanilino)-7-[5-(4-morpholinyl)-1-pentynyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloroanilino)-7-[(E/Z)-5-(4-morpholinyl)-1-pentenyl]-3-quinoline-carbonitrile,

35

- 4-(2,4-Dichloroanilino)-7-[5-(4-morpholinylmethyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloroanilino)-7-(3-hydroxy-1-propynyl)-3-quinolinecarbonitrile,
- 4-(2,4-Dichloroanilino)-7-[3-(dimethylamino)-1-propynyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloroanilino)-7-[(E/Z)-6-(4-morpholinyl)-1-hexenyl]-3-quinolinecarbonitrile,
- 7-[4,5-Bis(4-morpholinylmethyl)-2-thienyl]-4-(2,4-dichloroanilino)-3-quinolinecarbonitrile,
- 4-(2,4-Dichloroanilino)-7-[5-(2-pyridinyl)-2-thienyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,
- 7-[4,5-Bis(4-morpholinylmethyl)-2-thienyl]-4-(2,4-dichloro-5-methoxyanilino)-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(E)-3-(4-morpholinyl)-1-propenyl]-2-thienyl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[4-(4-morpholinyl)butyl]-2-thienyl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(4-morpholinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloroanilino)-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[3-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[2-(4-morpholinyl)ethyl]phenyl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{3-[2-(4-morpholinyl)ethyl]phenyl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-6-methoxy-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[2-(4-ethyl-1-piperazinyl)ethyl]phenyl}-3-quinolinecarbonitrile,
- 4-{3-Chloro-4-[(1-methyl-1*H*-imidazol-2-yl)sulfanyl]anilino}-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

37

7-[3,4-Bis(4-morpholinylmethyl)phenyl]-4-(2,4-dichloro-5-methoxyanilino)-3-quinolinecarbonitrile,

7-[3,4-Bis(4-morpholinylmethyl)phenyl]-4-{3-chloro-4-[(1-methyl-1*H*-imidazol-2-yl)sulfanyl]anilino}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-{3-[2-(4-morpholinyl)ethyl]phenyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-[3-(4-morpholinylmethyl]phenyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-{4-[2-(4-morpholinyl)ethyl]phenyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(1,3-dioxolan-2-yl)-3-thienyl]-3-quinoline-carbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(5-formyl-3-thienyl)-3-quinolinecarbonitrile,

4-(2,4-Dichloroanilino)-7-(5-formyl-3-thienyl)-3-quinolinecarbonitrile,

- 4-(2,4-Dichloro-5-methoxyanilino)-6-(5-formyl-3-thienyl)-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-3thienyl}-3-quinolinecarbonitrile,
- (2R)-1-({5-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]-2furyl}methyl)-2-pyrrolidinecarboxamide,
- 7-[5-(4-Morpholinylmethyl)-3-pyridinyl]-4-(4-phenoxyanilino)-3quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(4-morpholinylmethyl)-3-pyridinyl]-3quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-6-[5-(4-morpholinylmethyl)-3-thienyl]-3quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(1,3-dioxolan-2-yl)-2-thienyl]-3quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-(5-formyl-2-thienyl)-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(4-morpholinylmethyl)-2-furyl]-3quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[(E)-2-(4-methoxyphenyl)ethenyl]-3quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-2thienyl}-3-quinolinecarbonitrile,

- 7-[5-(4-Morpholinylmethyl)-2-pyridinyl]-4-(4-phenoxyanilino)-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(4-morpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-({[2-(phenylsulfonyl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-(1*H*-pyrrol-1-yl)-3-quinolinecarbonitrile,
- 4-(3-Bromoanilino)-6-(2-formyl-1*H*-pyrrol-1-yl)-3-quinolinecarbonitrile,
- 4-(3-Chloro-4-fluoro-phenylamino)-7-methoxy-6-(1*H*-pyrrol-1-yl)-3-quinolinecarbonitrile,
- 4-{3-Chloro-4-[(1-methyl-1*H*-imidazol-2-yl)sulfanyl]anilino}-7-(4-formylphenyl)-3-quinolinecarbonitrile,
- 4-{3-Chloro-4-[(1-methyl-1*H*-imidazol-2-yl)sulfanyl]anilino}-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{1-[2-(4-morpholinyl)ethyl]-1H-imidazol-5-yl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[4-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

40

4-(2,4-Dichloro-5-methoxyanilino)-7-[2-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[4-(4-morpholinyl)phenyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[4-(4-morpholinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(5-formyl-1-methyl-1H-pyrrol-2-yl)-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[1-methyl-5-(4-morpholinylmethyl)-1H-pyrrol-2-yl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{1-methyl-5-[(4-methyl-1-piperazinyl)methyl]-1H-pyrrol-2-yl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[1-methyl-5-({[2-(phenylsulfonyl)ethyl]amino}methyl)-1H-pyrrol-2-yl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[1-methyl-5-({[2-(methylsulfonyl)ethyl]-amino}methyl)-1H-pyrrol-2-yl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[5-({[2-(2-pyridinyl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,

- 7-(5-{[Bis(2-hydroxyethyl)amino]methyl}-2-furyl)-4-(2,4-dichloro-5-methoxyanilino)-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-({[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(1-piperidinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,
- 4-{2-Chloro-4-fluoro-5-methoxyanilino}-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-{2-Chloro-5-methoxy-4-methylanilino}-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[6-(4-morpholinylmethyl)-3-pyridinyl]-3-quninolinecarbonitrile,
- 7-[4,5-Bis(4-morpholinylmethyl)-2-thienyl]-4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-3-quinolinecarbonitrile,
- $4\hbox{-}(2,4\hbox{-}Dichloro-5\hbox{-}methoxy anilino})\hbox{-}7\hbox{-}(4\hbox{-}formylphenyl)\hbox{-}3\hbox{-}quino line carbonitrile,}$
- (2R)-1-{4-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzyl}-2-pyrrolidinecarboxamide,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[4-({[2-(phenylsulfonyl)ethyl]amino}methyl)-phenyl]-3-quinolinecarbonitrile,

42

4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[(dimethylamino)methyl]phenyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[(diethylamino)methyl]phenyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[4-({[2-(methylsulfonyl)ethyl]amino}methyl)-phenyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[2-(4-methoxyphenyl)ethynyl]-3-quinoline-carbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[2-(2-pyridinyl)ethynyl]-3-quinolinecarbonitrile,

 $\hbox{$4$-(2,4$-Dichloro-5-methoxyanilino)-7$-pyrrol-1-yl-3-quinoline carbonitrile,}\\$

4-(2,4-Dichloro-5-methoxyanilino)-7-{(2-[(dimethylamino)methyl]-1H-pyrrol-1-yl}-3-quinolinecarbonitrile,

7-[5-(1,3-Dioxolan-2-yl)-3-thienyl]-4-[3-methyl-4-(2-pyridinylmethoxy)anilino]-3-quinolinecarbonitrile,

4-[3-Methyl-4-(2-pyridinylmethoxy)anilino]-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

- 4-[(2,4-Dichloro-5-methoxyanilino]-7-(2-formyl-1-methyl-1H-imidazol-5-yl)-quinoline-3-carbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[4-(1-piperazinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{4-[(4-isopropyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- (E)-3-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]-2-propenoic acid,
- (1-{4-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzyl}-4-piperidinyl)acetic acid,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[4-(hydroxymethyl)phenyl]-3-quinolinecarbonitrile,
- 7-[4-(Chloromethyl)phenyl]-4-(2,4-dichloro-5-methoxyanilino)-3-quinolinecarbonitrile,
- 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-[4-(1H-1,2,3-triazol-1-ylmethyl)phenyl]-3-quinolinecarbonitrile,
- $4\hbox{-}(2,4\hbox{-}Dichloro\hbox{-}5\hbox{-}methoxyanilino)\hbox{-}7\hbox{-}(1H\hbox{-}pyrrol\hbox{-}2\hbox{-}yl)\hbox{-}3\hbox{-}quinoline carbonitrile,}\\$
- 4-[(2,4-Dichloro-5-methoxyanilino]-7-[4-(1H-tetraazol-5-yl)phenyl]-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-(5-{[(2-hydroxyethyl)(methyl)amino]methyl}-2-pyridinyl)-3-quinolinecarbonitrile,

44

Methyl 1-{[6-(4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-3-cyano-7-quinolinyl)-3-pyridinyl]methyl}-4-piperidinecarboxylate,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[5-(4-ethyl-1-piperazinyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[6-(4-morpholinylmethyl)-3-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[6-(4-thiomorpholinyl)-3-pyridinyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[3-(morpholin-4-ylmethyl)-pyridin-2-yl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(3-formyl)-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{3-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

 $4\hbox{-}(2,4\hbox{-}Dichloro\hbox{-}5\hbox{-}methoxy anilino})\hbox{-}7\hbox{-}(2\hbox{-}formylphenyl)\hbox{-}3\hbox{-}quino line carbonitrile,}$

4-(2,4-Dichloro-5-methoxyanilino)-7-[2-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(1-naphthyl)-3-quinolinecarbonitrile,

 $\hbox{$4$-(2,4$-Dichloro-5-methoxyanilino)-7$-(2-naphthyl)-3-quinoline carbonitrile,}\\$

N-{3-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]phenyl}acetamide,

7-(1-Benzofuran-2-yl)-4-(2,4-dichloro-5-methoxyanilino)-3-quinolinecarbonitrile,

7-(1-Benzothien-2-yl)-4-2,4-dichloro-5-methoxyanilino)-3-quinolinecarbonitrile,

4-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzoic acid,

4-(2,4-Dichloro-5-methoxyanilino)-7-(3-nitrophenyl)-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-6-methoxy-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

7-[3,4-Bis(4-morpholinylmethyl)phenyl]-4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-6-methoxy-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-6-methoxy-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-6-methoxy-7-{5-[(4-methyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-6-methoxy-7-(4-methoxyphenyl)-3-quinolinecarbonitrile,

4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-[4-(4-morpholinyl)phenyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[4-(4-morpholinylcarbonyl)phenyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[(2-methoxy)ethoxy]phenyl}-3-quinolinecarbonitrile,

4-(2-Chloro-5-methoxyanilino)-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-[4-(Benzyloxy)-3-chloroanilino]-7-[3,4-bis(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

7-[3,4-Bis(4-morpholinylmethyl)phenyl]-4-(2-chloro-5-methoxy-4-methylanilino)-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{4-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[4-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile,

tert-Butyl 4-{4-[4-({3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-3-cyano-7-quinolinyl]benzyl}-1-piperazinecarboxylate,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{4-[(4-morpholinyl)methyl]phenyl}-3-quinolinecarbonitrile,

 $\hbox{$4$-(2,4$-Dichloro-5-methoxyanilino)-7$-[(E)-2$-phenylethenyl]-3$-quinoline carbonitrile,}$

47

4-(2,4-Dichloro-5-methoxyanilino)-7-(2-phenylethynyl)-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[2-(4-methylphenyl)ethynyl]-3-quinolinecarbonitrile,

tert-Butyl (E)-3-[3-cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]-2-propenoate,

4-(2,4-Dichloro-5-methoxyanilino)-7-(3-hydroxy-1-propynyl)-3-quinolinecarbonitrile,

Ethyl (1-{4-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzyl}-4-piperidinyl)acetate,

Ethyl 1-{4-[3-cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzyl}-2-piperidinecarboxylate,

4-(2,4-Dichloro-5-methoxyanilino)-7-[3-(4-morpholinyl)-1-propynyl]-3-quinolinecarbonitrile,

1-{4-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzyl}-2-piperidinecarboxylic acid,

Ethyl 1-(4-{3-cyano-4-[(2,4-dichloro-5-methoxyphenyl)amino]-7-quinolinyl}benzyl)-3-piperidinecarboxylate,

1-(4-{3-Cyano-4-[(2,4-dichloro-5-methoxyphenyl)amino]-7-quinolinyl}benzyl)-3-piperidinecarboxylic acid,

48

4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-{4-[(1,1-dioxido-4-thiomorpholinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-{4-[(1-oxido-4-thiomorpholinyl)methyl]phenyl}-3-quinolinecarbonitrile,

7-(3-Chloro-1-propynyl)-4-[(2,4-dichloro-5-methoxyphenyl)amino]-3-quinolinecarbonitrile,

4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-[4-(4-thiomorpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-(4-morpholinylmethyl)-2-furyl]-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-(1-piperidinylmethyl)-2-furyl]-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-(5-formyl-2-furyl)-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-(1-piperidinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[5-(hydroxymethyl)-1-methyl-1H-pyrrol-2-yl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(3-formyl-2-thienyl)-3-quinolinecarbonitrile,

tert-Butyl 2-[3-cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]-1H-pyrrole-1-carboxylate,

7-[1,1'-Biphenyl]-4-yl-4-(2,4-dichloro-5-methoxyanilino)-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-[3-(4-morpholinyl)-1-propynyl]-3-quinolinecarbonitrile,

4-(4-Chloro-5-methoxy-2-methylanilino)-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

7-[4,5-Bis(4-morpholinylmethyl)-2-thienyl]-4-(4-phenoxyanilino)-3-quinolinecarbonitrile,

7-[4,5-Bis(4-morpholinylmethyl)-2-thienyl]-4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-formyl-2-pyridinyl)-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-pyridinyl)-3-quinolinecarbonitrile,

7-(3-Aminophenyl)-4-[(2,4-dichloro-5-methoxyphenyl)amino]- 3-quinolinecarbonitrile,

I-{[6-(4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-3-cyano-7-quinolinyl)-3-pyridinyl]methyl}-4-piperidinecarboxylic acid,

1-{6-[3-Cyano-4-(2,4-dichloro-5-methoxyphenylamino)-quinolin-7-yl]-pyridin-3-ylmethyl}-piperidine-4-carboxylic acid methyl ester,

1-{6-[3-Cyano-4-(2,4-dichloro-5-methoxyphenylamino)-quinolin-7-yl]-pyridin-3-ylmethyl}-piperidine-4-carboxylic acid,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-(5-chloro-2-pyridinyl)-3-quinolinecarbonitrile,

4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-[5-(4-ethyl-1-piperazinyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[5-(1-pyridinyl]-3-quinolinecarbonitrile,

51

- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-6-[5-(4-ethyl-1-piperazinyl)-2-pyridinyl]-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-6-[5-(4morpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-6-{5-[(4methyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-6-[6-(4morpholinyl)-3-pyridinyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[6-(4-morpholinyl)-3-pyridinyl]-3quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[2-(4-morpholinyl)-5-pyrimidinyl]-3quinolinecarbonitrile,
- 4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-(4morpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-2pyridinyl}-3-quinolinecarbonitrile,
- 4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-methyl-1piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,
- 4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[6-(4-morpholinyl)-3-pyridinyl]-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[2-(4-morpholinyl)-5-pyrimidinyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-3-

thienyl}-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-{6-[4-(4-morpholinylmethyl)phenoxy]-3-

pyridinyl)-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-(4-methoxyphenyl)-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[6-(4-ethyl-1-

piperazinyl)-3-pyridinyl]-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[6-(4-methyl-1-

piperazinyl)-3-pyridinyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[6-(4-ethyl-1-piperazinyl)-3-pyridinyl]-3-

quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[6-(4-methyl-1-piperazinyl)-3-pyridinyl]-3-

quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[6-(4-

morpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-7-[6-(4-morpholinylmethyl)-2-pyridinyl]-3-

quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{6-[(4-ethyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{6-[(4-methyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[4-(4-morpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-[4-(4-morpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{4-[(4-ethyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{4-[(4-methyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[3-(4-morpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{3-[(4-ethyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{3-[(4-methyl-1-piperazinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[4-(1-pyrrolidinyl)-1-piperidinyl]-3-pyridinyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[6-(1-piperidinyl)-3-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[(2-methoxyethyl)(methyl)amino]-3-pyridinyl}-3-quinolinecarbonitrile,

Ethyl 1-{5-[4-({3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-3-cyano-7-quinolinyl]-2-pyridinyl}-4-piperidinecarboxylate,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[6-(4-hydroxy-1-piperidinyl)-3-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[4-(2-hydroxyethyl)-1-piperazinyl]-3-pyridinyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[(2-hydroxyethyl)(methyl)amino]-3-pyridinyl}-3-quinolinecarbonitrile,

4-({3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-(5-{[4-(2-hydroxy-ethyl)-1-piperazinyl]-methyl}-2-pyridinyl)-3-quinolinecarbonitrile

4-(2,4-Dichloro-5-methoxyanilino)-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-(5-thiomorpholinylmethyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[(4-ethyl-1-piperazinyl)methyl]-3-pyridinyl}-3-quinolinecarbonitrile,

- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[(4-methyl-1-piperazinyl)methyl]-3-pyridinyl}-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-(6-formyl-3-pyridinyl)-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[(4-hydroxy-1-piperidinyl)methyl]-3-pyridinyl}-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-[6-(1-piperidinylmethyl)-3-pyridinyl]-3-quinolinecarbonitrile,
- 4-({3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]phenyl}amino)-7-{6-[(4-isopropyl-1-piperazinyl)methyl]-3-pyridinyl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[1-methyl-2-(4-morpholinylmethyl)-1H-imidazol-5-yl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-{1-methyl-2-[(4-methyl-1-piperazinyl)methyl]-1H-imidazol-5-yl}-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-(2-formyl-1-methyl-1H-imidazol-5-yl)-6-methoxy-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-[4-({[2-(2-pyridinyl)ethyl]amino}-methyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-Dichloro-5-methoxyanilino)-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

Methyl 1-{4-[3-cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzyl}-4-piperidinecarboxylate,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-[1-methyl-2-(4-morpholinylmethyl)-1H-imidazol-5-yl]-3-quinolinecarbonitrile,

4-(2,4-Dichloro-5-methoxyanilino)-6-methoxy-7-{1-methyl-2-[(4-methyl-1-piperazinyl)methyl]-1H-imidazol-5-yl}-3-quinolinecarbonitrile,

4-(2-Chloro-5-methoxy-4-methylanilino)-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-(2-Chloro-4-fluoro-5-methoxyanilino)-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-(2-Chloro-5-methoxyanilino)-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

1-{4-[3-Cyano-4-(2,4-dichloro-5-methoxyanilino)-7-quinolinyl]benzyl}-4-piperidinecarboxylic acid,

4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile.

Additionally, preferred compounds of the invention or a pharmaceutically acceptable salt thereof are:

4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[4-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(4-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(4-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{4-[(dimethylamino)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(4-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[4-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{3-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[3-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(3-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,

- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(3-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{3-[(dimethylamino)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[3-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(3-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{3-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[3-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[3-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{3-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(3-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-thienyl)-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

PCT/US01/09966

- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-pyridinyl]-3-quinolinecarbonitrile,
- 4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-pyridinyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{4-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 7-[4-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-4-(2,4-dimethylanilino)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(4-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(4-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-[4-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(4-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

- $4-(2,4-dimethylanilino)-7-[4-(\{[3-(4-morpholinyl)propyl]amino\}methyl)phenyl]-3-quinolinecarbonitrile,\\$
- 4-(2,4-dimethylanilino)-7-[4-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile
- 4-(2,4-dimethylanilino)-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{3-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 7-[3-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-4-(2,4-dimethylanilino)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(3-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(3-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-[3-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-[3-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(3-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-{3-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-[3-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-[3-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-{3-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-(3-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-furyl]-4-(2,4-dimethylamilino)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

- 4-(2,4-dimethylanilino)-7-[5-(4-morpholinylmethyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-[5-(1-piperidinylmethyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,
- 7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-thienyl]-4-(2,4-dimethylanilino)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-thienyl)-3-quinolinecarbonitrile,
- $4-(2,4-dimethylanilino)-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,$

PCT/US01/09966

4-(2,4-dimethylanilino)-7-[5-(4-morpholinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

WO 01/72711

4-(2,4-dimethylanilino)-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-3-thienyl]-4-(2,4-dimethylanilino)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-(5-{[(4-pyridinylmethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-(2,4-dimethylanilino)-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

- 4-(2,4-dimethylanilino)-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(5-{[(2-hydroxyethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-[5-(1-piperidinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,
- 4-(2,4-dimethylanilino)-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,

- 4-(4-bromo-2-chloro-6-methylanilino)-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-[5-(4-morpholinylmethyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-[5-(1-piperidinylmethyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-(4-bromo-2-chloro-6-methylanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

PCT/US01/09966

WO 01/72711

4-(4-bromo-2-chloro-6-methylanilino)-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-[5-(4-morpholinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-[5-({[3-(4-morpholinyl)propyl]amino}-methyl)-2-thienyl]-3-quinolinecarbonitrile,

4-(4-bromo-2-chloro-6-methylanilino)-7-[5-(1-piperidinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

4-({3-chloro-4'-[(4-hydroxy-1-piperidinyl)methyl]-5-methyl[1,1'-biphenyl]-4-yl}amino)-7-{4-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,

PCT/US01/09966

WO 01/72711

4-{[3-chloro-4'-({[2-(dimethylamino)ethyl]amino}methyl)-5-methyl[1,1'-biphenyl]-4-yl]amino}-7-[4-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-[(3-chloro-5-methyl-4'-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}[1,1'-biphenyl]-4-yl)amino]-7-(4-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[3-chloro-5-methyl-4'-(4-morpholinylmethyl)[1,1'-biphenyl]-4-yl]amino}-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4'-{[(2-hydroxyethyl)amino]methyl}-5-methyl[1,1'-biphenyl]-4-yl)amino]-7-(4-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-({3-chloro-5-methyl-4'-[(4-methyl-1-piperazinyl)methyl][1,1'-biphenyl]-4-yl}amino)-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{[3-chloro-5-methyl-4'-({[3-(4-morpholinyl)propyl]amino}methyl)[1,1'-biphenyl]-4-yl]amino}-7-[4-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-{[3-chloro-5-methyl-4'-(1-piperidinylmethyl)[1,1'-biphenyl]-4-yl]amino}-7-[4-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-({3-chloro-4'-[(4-ethyl-1-piperazinyl)methyl]-5-methyl[1,1'-biphenyl]-4-yl}amino)-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

69

PCT/US01/09966

4-[(3-chloro-4'-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-5-methyl[1,1'-biphenyl]-4-yl)amino]-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-({3-chloro-3'-[(4-hydroxy-1-piperidinyl)methyl]-5-methyl[1,1'-biphenyl]-4-yl}amino)-7-{3-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{[3-chloro-3'-({[2-(dimethylamino)ethyl]amino}methyl)-5-methyl[1,1'-biphenyl]-4-yl]amino}-7-[3-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-[(3-chloro-5-methyl-3'-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}[1,1'-biphenyl]-4-yl)amino]-7-(3-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-[(3-chloro-5-methyl-3'-{[(4-pyridinylmethyl)amino]methyl}[1,1'-biphenyl]-4-yl)amino]-7-(3-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

 $\label{lem:condition} $$4-{[3-chloro-3'-(\{[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-5-methyl[1,1'-biphenyl]-4-yl]amino}-7-[3-(\{[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,$

4-{[3-chloro-5-methyl-3'-(4-morpholinylmethyl)[1,1'-biphenyl]-4-yl]amino}-7-[3-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-[(3-chloro-3'-{[(2-hydroxyethyl)amino]methyl}-5-methyl[1,1'-biphenyl]-4-yl)amino]-7-(3-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-({3-chloro-5-methyl-3'-[(4-methyl-1-piperazinyl)methyl][1,1'-biphenyl]-4-yl}amino)-7-{3-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{[3-chloro-5-methyl-3'-({[3-(4-morpholinyl)propyl]amino}methyl)[1,1'-biphenyl]-4-yl]amino}-7-[3-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-{[3-chloro-5-methyl-3'-(1-piperidinylmethyl)[1,1'-biphenyl]-4-yl]amino}-7-[3-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-({3-chloro-3'-[(4-ethyl-1-piperazinyl)methyl]-5-methyl[1,1'-biphenyl]-4-yl}amino)-7-{3-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-[(3-chloro-3'-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-5-methyl[1,1'-biphenyl]-4-yl)amino]-7-(3-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-{2-chloro-4-[5-({[2-(dimethylamino)ethyl]amino}methyl)-3-thienyl]-6-methylanilino}-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-[2-chloro-6-methyl-4-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-3-thienyl)anilino]-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-[2-chloro-6-methyl-4-(5-{[(4-pyridinylmethyl)amino]methyl}-3-thienyl)anilino]-7-(5-{[(4-pyridinylmethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-{2-chloro-4-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-3-thienyl]-6-methylanilino}-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

71

4-{2-chloro-6-methyl-4-[5-(4-morpholinylmethyl)-3-thienyl]anilino}-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-(2-chloro-6-methyl-4-{5-[(4-methyl-1-piperazinyl)methyl]-3-thienyl}anilino)-7-{5-[(4-methyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-{2-chloro-6-methyl-4-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-3-thienyl]anilino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-{2-chloro-6-methyl-4-[5-(1-piperidinylmethyl)-3-thienyl]anilino}-7-[5-(1-piperidinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-(2-chloro-4-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-6-methylanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-[2-chloro-4-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-3-thienyl)-6-methylanilino]-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[4-({[3-(4-morpholinyl)propyl]amino}-methyl)phenyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

72

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[3-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(3-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(3-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[3-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{3-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

73

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-(4-morpholinylmethyl)-2-furyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-(1-piperidinylmethyl)-2-furyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-thienyl)-3-quinolinecarbonitrile,

74

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-(4-morpholinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[(4-pyridinylmethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[(2-hydroxyethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,

75

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-methyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-(1-piperidinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-[(3-chloro-4-phenoxyphenyl)amino]-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{4-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(4-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[4-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(4-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[4-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{3-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[3-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(3-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(3-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[3-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(3-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-(4-morpholinylmethyl)-2-furyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

78

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-(4-morpholinylmethyl)-2-thienyl]-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-methyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-thienyl]-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[(4-pyridinylmethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[(2-hydroxyethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-methyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-[5-(1-piperidinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(phenylsulfanyl)phenyl]amino}-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-{4-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,

- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-[4-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-(4-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-(4-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-[4-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-(4-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-[4-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-[4-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile,
- 4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

81

4-{[3-chloro-4-(3-furylmethyl)phenyl]amino}-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(4-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[4-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[4-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(4-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[4-(1-piperidinylmethyl)phenyl]-3-quinolinecarbonitrile,

7-{4-[(4-ethyl-1-piperazinyl)methyl]phenyl}-4-{[4-(3-furylmethyl)phenyl]amino}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(4-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-{3-[(4-hydroxy-1-piperidinyl)methyl]phenyl}-3-quinolinecarbonitrile,

82

7-[3-({[2-(dimethylamino)ethyl]amino}methyl)phenyl]-4-{[4-(3-furylmethyl)phenyl]amino}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(3-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(3-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[3-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[3-(4-morpholinylmethyl)phenyl]-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(3-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-{3-[(4-methyl-1-piperazinyl)methyl]phenyl}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[3-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

7-{3-[(4-ethyl-1-piperazinyl)methyl]phenyl}-4-{[4-(3-furylmethyl)phenyl]amino}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(3-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}phenyl)-3-quinolinecarbonitrile,

WO 01/72711

4-{[4-(3-furylmethyl)phenyl]amino}-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-pyridinyl]-4-{[4-(3-furylmethyl)phenyl]amino}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-pyridinyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-2-pyridinyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(5-{[(4-pyridinylmethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[5-(4-morpholinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(5-{[(2-hydroxyethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,

84

4-{[4-(3-furylmethyl)phenyl]amino}-7-{5-[(4-methyl-1-piperazinyl)methyl]-3-thienyl}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-[5-(1-piperidinylmethyl)-3-thienyl]-3-quinolinecarbonitrile,

7-{5-[(4-ethyl-1-piperazinyl)methyl]-3-thienyl}-4-{[4-(3-furylmethyl)phenyl]amino}-3-quinolinecarbonitrile,

4-{[4-(3-furylmethyl)phenyl]amino}-7-(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(4-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}phenyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(4-{[(4-pyridinylmethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[4-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(4-{[(2-hydroxyethyl)amino]methyl}phenyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[4-({[3-(4-morpholinyl)propyl]amino}methyl)phenyl]-3-quinolinecarbonitrile,

85

4-(2,4-dichloro-5-methoxyanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(5-{[(4-pyridinylmethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-furyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-furyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-(1-piperidinylmethyl)-2-furyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-furyl}-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-thienyl)-3-quinolinecarbonitrile,

86

4-(2,4-dichloro-5-methoxyanilino)-7-{5-[(4-ethyl-1-piperazinyl)methyl]-2-thienyl}-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(5-{[(4-pyridinylmethyl)amino]methyl}-3-thienyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-({[2-(1H-imidazol-4-yl)ethyl]amino}methyl)-3-thienyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-{5-[(4-hydroxy-1-piperidinyl)methyl]-2-pyridinyl}-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-({[2-(dimethylamino)ethyl]amino}methyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(5-{[4-(1-pyrrolidinyl)-1-piperidinyl]methyl}-2-pyridinyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-(5-{[(2-hydroxyethyl)amino]methyl}-2-pyridinyl)-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[5-({[3-(4-morpholinyl)propyl]amino}methyl)-2-pyridinyl]-3-quinolinecarbonitrile,

4-(2,4-dichloro-5-methoxyanilino)-7-[(5-{[4-(2-hydroxyethyl)-1-piperazinyl]methyl)-2-pyridinyl]-3-quinolinecarbonitrile,